

PARK (W-H.)

DIPHTHERIA

AND

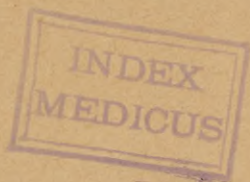
Allied Pseudo-Membranous Inflammations

A CLINICAL AND BACTERIOLOG-
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BY

WILLIAM HALLOCK PARK, M.D.

NEW YORK



Reprinted from the MEDICAL RECORD, July 30 and August 6,
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Diphtheria and Allied Pseudo-Membranous Inflammations.

*A CLINICAL AND BACTERIOLOGICAL STUDY.**

THE diagnosis of diphtheria has always been a subject of extreme importance in medicine.

Are all cases of diffuse pseudo-membranous inflammation of the upper air-passages, and all cases of membranous laryngitis, rhinitis, and tonsillitis the local manifestation of one disease—diphtheria? Are all these cases equally contagious and equally dangerous? These are questions which occur daily to the minds of practitioners.

The marked differences noticed in different cases have always forced on physicians the possibility that, under the term diphtheria, we may include more than one disease. When it was discovered that two different conditions existed in pseudo-membranous inflammations it was hoped that here we had a reliable diagnostic sign. One is a gangrenous inflammation, in which there is superficial necrosis, leaving on the removal of the adherent pseudo-membrane a bleeding surface; the other is an exudative inflammation, leaving on the removal of the loosely attached deposit an intact surface. The first was supposed to occur in true diphtheria, the second as a result of some local irritant, either chemical or bacteriological. Experience proved this test, like so many others, unreliable, and most clinical observers still thought it wisest to consider all pseudo-membranous inflammations as if they were the local expression of the acute infectious disease which we call diphtheria.

Since the discovery of the existence of bacteria, and of their relation to disease, a new hope has arisen that by the bacteriological examination of these pseudo-membranes we might get a truer knowledge of the disease

* Alumni Association College of Physicians and Surgeons Prize Essay, with additional cases.

called diphtheria, and settle the question, whether or no, under this name we should include more than one disease. At the outset the difficulties were very great, owing to the multitude of bacterial forms present in the mouth. However, persistent investigation, aided by the improved methods of bacteriological study, has overcome all these obstacles.

Although recent reviews by Loeffler,¹ Welch,² and others makes it almost unnecessary, it is thought best, in order to have the whole subject fresh in mind, to give as briefly as possible the reasons which have led to the acceptance of the Klebs-Loeffler bacillus as the cause of true diphtheria, this sketch to be followed by a summary of the chief characteristics of the bacillus, and the more important lesions produced by it. Finally, to present the evidence that a streptococcus is the most frequent agent of infection in cases of pseudo-membranous inflammation in which the Klebs-Loeffler bacillus is absent.

True Diphtheria.—In the year 1883, Klebs³ demonstrated, morphologically, the constant occurrence of a bacillus in the pseudo membranes of those subject to epidemic diphtheria. Loeffler,⁴ in 1884, published the results of a very thorough and extensive series of investigations. He found the bacillus described by Klebs in the pseudo-membranes in nearly all cases examined. He proved by inoculating that this bacillus was pathogenic in certain animals. When inoculated on the injured mucous membrane it produced a pseudo-membrane somewhat like that present in human diphtheria. He failed to find the Klebs bacillus either in the blood or organs of fatal cases of human diphtheria, or in the same regions of animals dying after inoculation. He came to the conclusion that the Klebs bacillus was the probable cause of true diphtheria. He considered, however, that further investigations were necessary to prove his conclusion.

Since then the whole subject has been examined with great care, not only by Loeffler himself, but also, independently, by a large number of investigators, both in Europe and America. The work of Roux and Yersin,⁵ in Paris; Loeffler, in Berlin; Kolisko and Paltauf,⁶ in Vienna; Ortmann,⁷ in Königsberg; Zarniko,⁸ in Kiel; Escherich,⁹ in Munich; Beck,¹⁰ Brieger,¹¹ and Fraenkel,¹² in Berlin; Tangl,¹³ in Tübingen; Babes,¹⁴ in Bucharest; d'Espine,¹⁵ in Geneva; Klein,¹⁶ in London; Welch and Abbott,¹⁷ in Baltimore; Prudden,¹⁸ in New York, and many others, has established that in all cases of typical infectious diphtheria the Klebs-Loeffler bacilli are present in large numbers in the pseudo-membranes, either alone or associated with other bacteria, and that the Klebs-Loef-

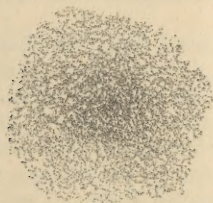
fler bacilli in all other inflammations of the throat and in healthy throats are very rarely found.

Pseudo-membranes, paralysis, and organic lesions can be produced in inoculated animals, similar to those found in human diphtheria. A toxine is produced by the bacilli which, when isolated and inoculated, produces the same results, with the exception of the pseudo-membrane, as the pure cultures.

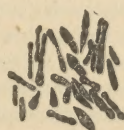
All the conditions have now been fulfilled which are necessary to the proof of the dependence of true diphtheria upon the bacilli described by Klebs and Loeffler.

The Klebs-Loeffler Bacilli.—They are moderate-sized rods, usually slightly bent, averaging nearly as long as the tubercle bacilli, but twice as broad and usually with rounded ends. According to the rapidity of growth, the soil, and other conditions, the form and size of the micro-organisms varies, and the differences are striking in appearance. The bacteria are sometimes enveloped in a more or less capacious membrane; sometimes the contents divide into a number of pieces, separated by transverse divisions; one end of the rods is frequently thickened like a club, or both ends may be clubbed, or one or both pointed. The bacilli are immobile and have no spores. The best staining agent is Loeffler's alkaline methyl blue. Some forms stain uniformly, others in various irregular ways, the most common being the appearance of deeply stained granules in a slightly stained bacillus, or of darkly stained ends with a paler centre. The bacilli are very often in pairs, never in chains; they are semi-anaërobic, and thrive only at a somewhat high temperature, 20° to 42° C.

The Loeffler bacilli can be cultivated upon all the ordinary culture-media, but grow most vigorously on a



Surface Colony of Klebs-Loeffler Bacilli, on Agar Plate, slightly magnified; twenty hours' growth.



Klebs-Loeffler Bacilli, highly magnified.

mixture of blood serum and nutrient bouillon, as given by Loeffler. On this, solidified, the bacilli grow as large, round, elevated, grayish-white colonies, with the centre more opaque than the somewhat irregular periphery.

The Sections of Diphtheritic Membrane show on the surface and in the most superficial portions of the pseudo-membrane Loeffler bacilli mixed with more or less numerous other micro-organisms. In the middle and deeper portions the Loeffler bacilli, alone or associated with streptococci, are usually the only organisms present. In the deepest layer there are very few bacilli and in the mucous membrane, as a rule, none. Extremely rarely they are found in the blood and viscera. Some of those bacteria which are associated with the Klebs-Loeffler bacilli in diphtheria, especially the streptococci, may be found in the mucous membrane, lymphatic glands, and internal organs.

Toxic Albumins.—The toxic albumins produced by the diphtheria bacilli have been especially investigated by Roux and Yersin,¹⁹ and Fraenkel and Brieger.²⁰ This toxic substance is of a proteid nature, precipitated by alcohol, soluble in water. Nearly pure, it is a white, amorphous mass of light specific gravity, and keeps its properties for a long time unchanged. Its extraordinary poisonous nature is shown by Roux and Yersin, in that four-tenths of a milligramme of the substance, when inoculated, was sufficient to kill eight guinea-pigs. If this poison be inoculated into a guinea-pig, it produces all the changes, except the pseudo-membrane, that the pure culture of the bacilli does. The long continuance of the toxic power of the poison in the body and its slow absorption from the locally infected tissues account for the deaths which occur some time after the entire disappearance of the bacilli from the infected throats.

The toxalbumin of diphtheria is very little, if at all, absorbed by intact mucous membranes, and can be swallowed by susceptible animals in large amounts, without danger.

Lesions.—In animals inoculated with the bacilli or these toxalbumins we find at the seat of inoculation a grayish focus surrounded by an area of congestion. The subcutaneous tissues for an extensive area around are congested and more or less oedematous. The adjacent lymph-glands are swollen and the serous cavities usually contain an excess of clear or turbid fluid. The microscopical changes in the internal organs of animals dying of experimental diphtheria have been studied by Babes,²¹ Welch²² and Flexnor, and others.

In the liver there are found numerous smaller and larger masses of necrotic cells. These areas are permeated by leucocytes. Congestion with hemorrhages into the capsule and tissue are present. In the kidneys fatty changes occur in the epithelium of the tubes and glome-

ruli and a hyaline alteration of the glomerular capillaries and of the smaller arteries. In the spleen and lymph-glands the necrosis of cells is also present. Both the cell-bodies and nuclei of living cells are altered. The lungs show areas of intense congestion with hemorrhages into their tissue. The heart is nearly always the seat of fatty degeneration. The fibres of the voluntary muscles show degenerative changes. The number of leucocytes is greatly increased in the blood.

Experimental Immunity.—The exceedingly interesting results obtained by Fraenkel, Behring,²³ Brieger,²⁴ and others²⁵ in producing immunity in animals, gives the hope at least of practical results in the future. They found that the blood or serum of animals rendered immune against diphtheria had the power of rendering other animals, when injected into their bodies, also immune. In animals already infected the injections had the power of destroying or neutralizing the poison secreted by the bacilli. It was also found that the offspring of immune animals possessed a considerable degree of immunity. Their success in treating animals has been so great that the endeavor to cure human diphtheria is soon to be made.

Duration of Life in the Klebs-Loeffler Bacilli.—The life of the bacillus varies greatly according to the conditions under which it is placed. An agar tube-culture in the laboratory is still alive after seven months' growth, and a bit of membrane no larger than a pin's head still gives cultures of both the bacilli and the streptococci four months after its removal from the throat. Some have found bits of membrane kept in cloth to be still alive after six months. Probably in dark, damp, dirty places life remains even longer, while, on the other hand, under unfavorable conditions the bacilli may live only a few days.

The Conditions Necessary for the Infection of Man with the contagium of diphtheria are of great practical importance. Whether this can be implanted on the normal mucous membrane in man is still a question. Undoubtedly a lesion favors it. When the Klebs-Loeffler bacilli are implanted on the normal mucous membranes of susceptible animals they do not grow. The researches of Barbier²⁶ throw interesting light on this subject. He found that a streptococcus which was associated with the Loeffler bacillus in all cases where marked redness and swelling were present, when implanted on the normal mucous membrane of the vagina in guinea-pigs, produced an acute purulent discharge, with redness and swelling. If with these cocci, or even four weeks later, the Loeffler bacilli were brought into contact with the mucous mem-

brane, a severe diphtheritic inflammation was started which often caused death. If these results can be applied to man, they add a new importance to the discovery that streptococci are frequently present in slightly inflamed throats, and to their frequent association in the pseudo-membranes with the Loeffler bacilli.

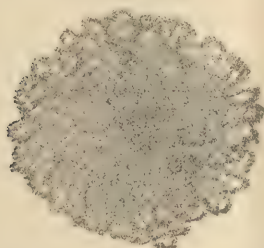
Pseudo-Diphtheria Bacillus.—The relation of this bacillus to that of true diphtheria is of much practical importance. Abbott²⁷ has recently given such an exhaustive review of this subject that it will only be necessary here to give a brief summary. The term is now used to define a group of bacilli which closely resemble the Loeffler, but which are without pathogenic properties in guinea-pigs. By some writers the term is used to cover varieties that show quite marked cultural and morphological differences.

It has been established that bacilli with all the characteristics of the Klebs-Loeffler, except their virulence, are to be found exceptionally where pseudo-membranes are absent. These are never numerous, only a few scattered colonies being found on plates or tubes. In some localities they are found rather frequently, in others rarely, or not at all. Roux and Yersin²⁸ found also that among those obtained from cases of diphtheria there were gradations in virulence from those whose inoculation caused death in guinea-pigs in twenty-four hours to those which produced only local changes. They found that those taken from mild cases are, as a rule, the least virulent. Beck found in some cases of true diphtheria both virulent and non-virulent bacilli.

As the result of a large number of experiments, Roux and Yersin hold that the morphological and cultural differences between the diphtheria and the pseudo-diphtheria bacilli are inconstant, and, when present, are insufficient to establish that they belong to different species. In this country the pseudo-diphtheria bacilli have been infrequently found. Prudden, in a large number of cases in New York, did not find them once. Koplik has found them a few times, and Abbott in fifty-three cases in four. In these studies the pseudo-diphtheria bacilli were met with only once, as proved by animal experiments. This whole subject needs further study.

For bedside diagnosis all cases which give typical colonies of bacilli resembling the Klebs Loeffler should be regarded as true diphtheria; both because of the length of time consumed in animal experiments and of the impossibility of being sure that because the colony from which the inoculating culture was made was not virulent all the colonies were the same. This merely compels a few doubtful cases of diphtheria to be still considered as such.

Pseudo-membranous Inflammations in which the Klebs-Loeffler Bacillus is Absent.—The presence of streptococci in the pseudo membranes and in the blood of fatal cases of diphtheria has been known for many years. Loeffler,²⁹ in 1884, described a class of cases where loss of substance with a gray yellow or necrotic base was a characteristic feature in which the Klebs-Loeffler bacillus was absent, but a streptococcus very abundant. He concluded that in these cases the frequency of the presence of the streptococci either means that the poison of diphtheria has been at first present, and thus prepared the way for the streptococci, and then vanished before examination, or that the streptococci are the cause of this peculiar form of pseudo-membranous inflammation. He came to the conclusion that the first supposition was the true one, that the streptococci were secondary to the Klebs-Loeffler bacilli.



Streptococcus Colony, slightly magnified ;
twenty hours' growth.



Streptococci, highly magnified.

This streptococcus he isolated in three cases from the tonsils and in two cases from the internal organs. Both the biological characters and the general effects upon inoculated animals seemed to indicate a close relationship with the streptococcus pyogenes and erysipelatus. The changes produced upon the mucous membrane by its inoculation did not resemble closely the characteristic local lesions of diphtheria. From that time until the present year it seemed to be the aim in Europe, especially in Germany, to seek out for examination only typical cases of epidemic infectious diphtheria. In these cases the Klebs-Loeffler bacilli were constantly found, and they came to be looked upon more and more as the only etiological cause of all extensive pseudo-membranous inflammations, at least when they were not complications of infectious diseases.

In 1889, Prudden³⁰ published the results of a very careful bacteriological investigation of twenty-four cases of fatal pseudo membranous inflammation of the tonsils, pharynx, and larynx, which were all considered clinically

to be diphtheria. These cases were mostly young children in two asylums where they had been exposed to scarlet fever and measles, and in some of whom these diseases had existed as a complication. In not one of these were the Klebs-Loeffler bacilli found, but in all but two streptococci. These were present in most of the cases in enormous numbers, as shown by the cultures. In three cases in which the viscera were examined they were found to contain a moderate number of streptococci. In the ducts of the mucous glands and in the lymph-spaces of the submucosa, the streptococci were found in greater or smaller numbers, also rarely in the tracheal and bronchial glands. The staphylococcus pyogenes aureus and albus were present in varying numbers, but hardly more frequently than in many apparently normal throats.

In sixteen of the twenty-four cases, broncho-pneumonia³¹ was present, and cultures made from the fresh broncho-pneumonic areas in fifteen of these gave large numbers of streptococci. The streptococci obtained from all these cases presented the same morphological and biological characters. They appeared to be identical with the streptococcus pyogenes.

From his investigations Prudden concluded that in a certain class of cases pseudo-membranes were caused by streptococci. Kolisko and Paltauf, Wurz and Bourges,³² Sevestre,³³ Tangl,³⁴ Baginsky,³⁵ and others have found streptococci but no Loeffler bacilli in the pseudo-membranous inflammations occurring early in scarlet fever. Baginsky,³⁴ in his recent studies, found that in one hundred and fifty-four cases clinically diagnosed as diphtheria, there were thirty-four in the pseudo-membranes of which no Loeffler bacilli were present. In two cases of membranous rhinitis he found the bacilli present. These ran the usual mild course.

Martin,³⁶ in Paris, has just published a clinical and bacteriological study of the croupous deposits of two hundred children suspected of diphtheria. He found in seventy-two no Klebs-Loeffler bacilli; of these, twenty-nine were croup cases. The mortality of these was far less than in those having true diphtheria. Some of the children had been exposed to scarlet fever and measles. He is of the opinion that the certain clinical diagnosis of these cases is impossible. A few examples of infection with diphtheria in the wards are given. He regards the association of different bacteria with the Loeffler bacilli as greatly modifying the course of the disease. As he used only blood-serum tubes, he probably has often overlooked the almost invisible colonies of the streptococci. He also believes that from the form of the

Klebs-Loeffler bacilli one can judge somewhat of their virulence.

Aim and Scope of these Investigations.—The object of these studies has been to determine by the bacteriological examination of a large number of cases whether, in fact, pseudo membranous inflammations can be divided into two distinct classes, and, if so, in what proportion of the cases the Klebs-Loeffler bacilli are present; also to go further and see if, by combining in all cases a very careful clinical examination with a bacteriological one, it would not be possible to find some constant differences between the local appearances and general symptoms of true diphtheria and those pertaining to other croupous inflammations.

The cases recorded in the following pages include all those having pseudo-membranous inflammations admitted to the wards of the Willard Parker Hospital during four consecutive months; also a number sent to me by several physicians, and six cases of membranous rhinitis from the throat classes of the Vanderbilt Clinic and the Roosevelt Hospital.

In all, one hundred and fifty-nine were examined; these will be studied in the following classes: True diphtheria, those in which the Klebs-Loeffler bacilli are present alone or with other bacteria; pseudo-diphtheria, those in which the Klebs-Loeffler bacilli were never present, but some form of cocci, usually streptococci.

For comparison, the following were also examined bacteriologically: Follicular tonsillitis, 10; peritonsillar abscess, 5; acute pharyngitis, 5; chronic pharyngitis, 5; hyperæmic throats in scarlet fever, 10.

Technical Observations.—To obtain the material for examination two methods were employed. Where a piece of membrane could be removed without injuring the throat, this was done by means of a long, slender pair of forceps, carefully sterilized. For the cases in which this was impossible, a number of cotton plugs* had been prepared by wrapping small portions of absorbent cotton around the ends of slender sticks, one inch in length, which were then placed in a tube and sterilized by dry heat. Taking one of these in the forceps, it was rubbed gently, but rather firmly, against any visible pseudo-mem-

* In a number of trials, in which, from the same cases, plates were made both from bits of membrane and from the swabs,* the latter proved as trustworthy as the former. For the use of physicians, who supplied me with cases from outside the hospital, I kept a number of strong glass tubes, two and one-half inches in length by one-half inch in thickness. Each tube contained an absorbent cotton swab, and was plugged with cotton. The tubes and their contents were then placed in the hot-air sterilizer. These could be carried in the pocket. After use at the bedside they were returned to the laboratory, where the plates and tubes were made.

brane ; when none was present, the cotton was rubbed against the tonsils and pharynx. The bit of membrane or cotton plug was then gently drawn three or four times across the surface of a six per cent. glycerine-agar Petri plate, making equally distant lines of inoculation. Taken to the laboratory, here the bit of membrane or swab was drawn across a blood-serum tube and then rubbed in a few drops of sterilized water. With a sterilized platinum loop a drop of this turbid fluid was taken up and drawn across two or more solidified Loeffler's blood-serum tubes, and a second drop across a second agar plate. The tubes and plates were placed in the thermostat and kept at 37° C. for twenty-four hours. From the membrane, or swab, two cover-glass smears were prepared, stained with Loeffler's methyl blue solution, studied under the microscope, and the forms of bacteria seen recorded. On the following day the colonies of the Loeffler bacilli, when present, in every case had reached a size sufficient to be distinctly seen on both the blood-serum tubes and agar plates, and, under the microscope, showed their extremely characteristic appearance on the latter.

It is necessary to be extremely careful to have the glycerine agar faintly alkaline, to have proper peptone, and to use only fresh, moist plates, otherwise there may result an entire failure to get any growth of the Loeffler bacilli.

In these investigations the special object in view was to discover in the cultures the presence, or absence, as well as the relative abundance of the Klebs-Loeffler bacilli, the streptococci, and the staphylococci. Any other forms of bacteria that appeared frequently or in large numbers were also investigated.

The Comparative Value as Culture-media of Blood-serum and Six-per-cent. Glycerine-Agar.—On the solidified blood-serum mixture suggested by Loeffler the Klebs-Loeffler bacilli grow more rapidly and surely than on any other of the usual solid media. The growth of the colonies, though fairly uniform, is not sufficiently characteristic to certainly identify them, for certain frequently present cocci grow with almost the same rapidity and appearance. The usefulness of the serum is limited to tubes, from its slight cloudiness and the great difficulty of making plates.

On glycerine-agar the growth of the bacilli is less rapid, but still vigorous when made from fresh bits of membrane or swabs. The gross appearance of the colonies is here also very similar to those of several forms of cocci. The appearance of the colonies under the microscope is, on the other hand, extremely characteristic and entirely different from those of any other bacteria occurring in the throat, with the possible exception of the pseudo-diphtheria bacilli. Glycerine-agar in tubes is



1



2



3



4



5



6

PHOTOGRAPHS OF PLATE CULTURES FROM DIPHTHERIA AND SCARLATINA.—PARK.

much less useful than the serum, but in plates it has many great advantages, and if it were not that under certain conditions, when still capable of growing on the blood serum, the Loeffler bacilli are unable to grow on the agar, the agar plates could entirely replace the serum tubes. This absence of growth on agar has occurred in two cases where frequent irrigation with 1 to 4,000 bichloride of mercury had been employed, also from two long-dried swabs.

In disinfection work, cultures would be obtained on blood serum when they no longer appeared on the agar. With these exceptions the plates always contained colonies of the Loeffler bacilli whenever the tubes contained them.

Throat cultures show the most characteristic growth under the microscope when the plates are examined after remaining from sixteen to twenty-four hours in the thermostat. The colonies of the different bacteria common to the throat have then attained a characteristic growth and are still for the most part distinctly separate. At this time, after some familiarity with the work, you can rapidly run over the plates, placed under the microscope, with a low power lens, and acquire a knowledge not only of how many varieties of organisms are present but also the relative proportion. The colonies can then be further studied by a higher power lens and under the microscope accurately fished.

For the photographs of six of the plate cultures, shown in the accompanying Plate, I have to thank my friend Dr. Edward Leaming. These give the usual appearance of the plates made from fresh membranes or swabs. At times the colonies are much closer together, at other times less so than in these. They show at a glance the actual and relative size of the colonies, and to some extent their appearance after twenty to thirty hours' growth at 37° C. It can be readily seen how thoroughly the isolated colonies can be investigated when the uncovered plate is put on the microscope-stand and each colony individually studied with any power lens desired.

EXPLANATION OF PLATE.

Figs. 1 and 2 show cultures from same diphtheritic membrane—1, with numerous; 2, with fewer colonies. The more numerous colonies are composed of diphtheria bacilli; the larger whiter ones of non-pathogenic bacilli.

Fig. 3, pure culture of diphtheria bacilli from tissue of inoculated guinea-pig.

Fig. 4, culture obtained by pressing a portion of a soiled sheet, removed from a diphtheria patient, against the media surface. Many varieties of bacteria grew. The smaller colonies are diphtheria bacilli and streptococci.

Fig. 5, a pure culture of streptococci from scarlatinal membrane.

Fig. 6, culture from croupous tonsillitis. The exceedingly small colonies are streptococci. Some of moderate size, staphylococci. No diphtheria. In both 5 and 6 the condensation water has swept the bacteria over the plate surface, making a diffuse growth of colonies.

Glycerine-agar plates in which the media has been tested are sufficient when the cultures are to be made immediately from throats in which frequent antiseptic irrigation has not been used. Whenever the bacilli may have been injured from antiseptics, drying, or any other cause, the blood-serum tubes should also be used to insure the growth of the Loeffler bacilli.

For the simple determination of the presence or absence of the Loeffler bacilli the blood-serum suffices. I believe that the failure to fully recognize that there are many extensive pseudo-membranes, neither due to the Loeffler bacillus nor occurring after scarlatina, is owing to the almost exclusive use of blood serum tubes, since in tubes it is impossible to satisfactorily use the microscope to identify the smaller colonies, and before they become visible to the eye they are often overgrown by the more rapidly growing bacteria.

When the colonies of the bacteria sought for were plainly isolated, tube cultures were immediately made from a characteristic colony; when not, a sowing was made on a fresh plate and isolated colonies obtained.

Animal Inoculations.—From the first or second generation of the Klebs Loeffler bacilli, tubes of faintly alkaline nutrient bouillon were inoculated. The tubes were removed from the thermostat on the fourth day. Two-thirds of the clear bouillon was poured off and the remainder well shaken. One-third cubic centimetre of this fluid, turbid with the bacilli, was inoculated into the subcutaneous tissue of the side of the abdomen of a guinea-pig. Guinea-pigs were inoculated from cultures of twenty-two of the cases in which the Klebs-Loeffler bacilli were present. In nineteen death followed with typical pathological changes. In no case were the bacilli, or any other bacteria, obtained in the cultures made from the heart's blood, the liver, or spleen. In no case were any other pathogenic bacteria than the Klebs-Loeffler bacilli obtained from the cultures made from the oedematous fluid and congested tissue in the immediate neighborhood of the point of inoculation.

The temperature in the animals fell after inoculation in every case but one, in which a temporary rise occurred, and remained from one to three degrees below the normal until death.

The streptococci taken from four cases of true diphtheria and from four cases of pseudo-membranes in which the Loeffler bacilli were absent were inoculated in rabbits. The temperature of the rabbits rose after inoculation, in every case, from one to five degrees. In two local abscess and sloughing of tissue occurred. In three temporary swelling and redness and in three no reaction

appeared. Four died between the fourth and fifth weeks. No streptococci were obtained from either the blood or viscera of the fatal cases.

Description of the Willard Parker Hospital.—This hospital is under the control of the New York City Board of Health and to it are sent diphtheria and scarlet-fever cases. The diphtheria wards, in which the majority of the cases here studied were treated, comprise three large, high rooms, connected by a hallway. Two are used for the women and children, and one for the men. As far as possible, the convalescent and doubtful cases are separated from those having true diphtheria; but owing to the frequently crowded condition of the wards, this often cannot be done. The floors are of hard wood, and are washed daily with 1 to 1,000 bichloride solution. The iron bedsteads are carbolized each morning. Where patients soil their beds, the sheets and spreads are changed daily; in other cases, weekly. All patients have their nostrils and throats syringed with a 1 to 4,000 bichloride solution, the bad cases every half hour, the convalescents three times a day. No swabbing of throats is allowed. All clothes brought to the hospital are disinfected, and are only returned when patients leave. Patients are also required to take a bath when they go (also, if possible, when they come), washing the hair with a 1 to 1,000 bichloride of mercury solution.

Cases of laryngeal dyspnoea when urgent, or when not relieved by vomiting and calomel fumigations, are intubated. The only routine constitutional treatment is to give alcoholic stimulants throughout the course of the disease to those showing any tendency to heart failure. Tube cases are fed lying on the lap with lowered head. These details are necessary to show the conditions under which the patients were placed, and to avoid a repetition of the account of the treatment in the clinical histories which follow. The wards for scarlet fever are on a different floor, and have the same arrangement of rooms.

Methods of Clinical Study.—I made daily rounds with Dr. Lester, the resident physician; each case was carefully observed, the appearance of the throat, and the complicating conditions of the larynx and nostrils were noted. As far as possible sketches were made, and the changes occurring from day to day noticed. The figures for pulse, temperature, and respiration were taken from the hospital charts—the temperature in children being always taken by the rectum, in adults by axilla. The urine analyses were also obtained from the hospital records. Cultures were made from every case on the day of admission, those which showed very numerous col-

onies of the Loeffler bacilli were not examined again for three days, and then every other day till the bacilli had twice proved absent. Cultures were made twice from cases of croupous tonsillitis. Those having croupous laryngitis were examined daily, until all doubt as to the presence or absence of the Loeffler bacilli was dispelled, swabs and bits of coughed-up membrane being used. The same care was taken in extensive pseudo-membranous inflammations, in which the Loeffler bacilli were absent. During the last six weeks some of the cases were subjected to only one thorough bacteriological examination.

True Diphtheria (Clinical histories and bacterial examinations of 27 illustrative cases from the 54 in which the Klebs-Loeffler bacilli were present).—The aim is to present in the histories only the most important points.

CASE I. February 6th.—Molly F—, aged five; membranous laryngitis; intubation; death. Clinical history: Well nourished; admitted with marked laryngeal dyspnoea; slight adherent patches on tonsils; no pain on opening mouth; no swelling of glands of neck. Temperature, 101° F.; pulse, 118; respiration, 34. Vomiting and fumigations not relieving the dyspnoea, she was intubated.

February 9th.—Temperature has remained between 100 and 101° F.; pulse and respiration remain about the same. Patient is very languid, and has at times dyspnoea, which is relieved by calomel fumigations. Patches still remain on tonsils.

February 12th.—Tonsils clean. Condition unchanged.

February 18th.—Temperature normal. Tube removed.

March 2d.—Patient taken home; she is weak, can hardly stand, and cannot speak above a whisper. Since the tenth day considerable quantities of albumin have been present in the urine. Considerable emaciation.

March 11th.—Patient returned for laryngeal dyspnoea, apparently due to laryngeal paresis. She was intubated.

March 24th.—Tube removed. Patient is anæmic; muscles are somewhat atrophied; some albumin persists in urine. Remains in bed.

March 28th.—Is sitting up and gaining slightly in strength. Returned home. Died two weeks later at home, apparently from nephritis.

Bacterial examination: Cover glass smear showed many fairly typical Loeffler bacilli. Plates and tubes showed almost a pure culture of vigorous growing colonies of the Klebs-Loeffler bacilli. A colony was re-plated, and from this new growth a bouillon tube was inoculated. A guinea-pig inoculated with $\frac{1}{8}$ c.c. of bouillon culture died in forty-three hours with characteristic lesions. A pure culture of the Loeffler bacilli was

obtained from the tissue at seat of inoculation, while the plates from the heart and organs were sterile.

CASE II. February 29th.—Harry S—, aged two; intubation; membranous laryngitis; recovery. Clinical history: Admitted with marked laryngeal dyspnoea. Intubation gave complete relief. No membrane visible anywhere in throat. Very slight prostration. Temperature, 101° F.; pulse, 124; respiration, 32. On sixth day tube was coughed up. Except for the slight prostration there were no bad symptoms.

Bacterial examination: Plates and tubes made from a swab of the throat contained a number of typical colonies of the Klebs-Loeffler bacilli. Cultures made on following days gave none. Streptococci were always present. Guinea-pig died in forty-eight hours with characteristic lesions.

CASE III. February 20th.—Sarah S—, aged four; intubation; death. Clinical history: The child had been intubated before admission; heart irregular and weak; a few grayish semi-adherent patches on tonsils. Temperature, 100.6° F.; pulse, 134; respiration, 42.

February 22d.—Breathing badly, swallows with difficulty. Died, 7.15 P.M.

Bacterial examination: Plates show many typical colonies of Loeffler bacilli, and many of streptococci.

CASE IV. February 23d.—Benjamin J—, aged two years and ten months; intubation; death; extensive membrane. Clinical history: Thick, greenish-gray, adherent pseudo-membrane on uvula, anterior faucial pillar and pharynx; croupy; glands of neck swollen. Temperature, 101° F.; pulse, 126; respiration, 38. Very restless.

February 26th.—Intubated, with relief of laryngeal dyspnoea.

February 27th.—Heart failure and death.

Bacterial examination: Plates revealed a great number of active growing colonies of the Loeffler bacilli, and some of streptococci. Guinea-pig inoculated died between forty-eight and sixty hours with characteristic changes.

CASE V.—Private case, aged one; intubation; death; extensive membrane. Clinical history: Soft, grayish, pseudo-membranous patches on tonsils, base of uvula, and in nostrils. Temperature, 101° F.; pulse, 120. Membrane spread slowly over pharynx, and on fifth day invaded the larynx; dyspnoea gradually increased; tissues of neck became greatly swollen; intubated with but slight relief. Died on seventh day. Temperature never above 102° F.

Bacterial examination: Many colonies of the Loeffler bacilli and of streptococci.

History of infection: Three days before first symp-

toms child had been put in a crib for a few hours, occupied, two weeks before, by a child who had passed through a dangerous attack of diphtheria.

CASE VI. February 28th.—Rachel M——, aged five. Death after disappearance of the membrane. Clinical history: Both tonsils, anterior pillars, left side of uvula, and soft palate covered by a thick, firmly adhesive, grayish pseudo-membrane. Dirty discharge from nose. Temperature, 99° F.; pulse, 110; respiration, 24. Apathetic.

March 1st.—Croupy, relieved by calomel fumigation. Temperature, 99.5° F.

March 7th.—Thick membrane has separated. Superficial ulceration on faucial pillars and tonsils covered by thick purulent discharge. Since the third the urine has contained large amounts of albumin. Is very weak and apathetic. Speaks in whispers and swallows with difficulty.

March 15th.—Copious discharge continued, and patient seems unable to swallow or spit it up. Patient suddenly began to breathe with feeble gasps and died at 7.30 A.M.

Bacterial examination: Cover glass from smear gave an almost pure culture of typical Loeffler bacilli. Cultures gave a large number of colonies of the Loeffler bacilli, and a smaller number of colonies of micrococci which appeared as diplococci and in rows of two to eight. After the disappearance of the membrane no more Loeffler bacilli were present, the micrococci above noticed and many other forms replacing them.

Guinea-pig died in forty-eight hours with characteristic lesions.

Cases 7 to 10 in one family. Malignant diphtheria.

CASE VII. March 6th.—Cora B——, aged twenty-six, the mother; died. Clinical history: Has been sick five days. Uvula, posterior fauces, tonsils and pharynx greatly swollen and covered by a very thick, yellow-gray membrane, nostrils occluded by membrane. Lymph-glands hard, slightly swollen. Temperature 100.8° F.; pulse, 106 and feeble; respiration, 26. Is apathetic, can hardly swallow or whisper. Feels that she is choking.

March 8th.—No improvement. Nasal passages obstructed by thick membrane; sweetish, offensive odor. Can hardly swallow or spit up the copious discharge. Patient grew worse on the 10th. Pulse became imperceptible and death occurred at 4 P.M.

CASE VIII. March 6th.—Maud B——, aged five, daughter of last; death after disappearance of membrane. Clinical history: Sick for three days. At base of uvula and on tonsils are large patches of thick, yellowish-gray pseudo-membrane. Nasal passages occluded by thick, fibrinous membrane. Same odor as from mother.

Slightly* croupy. Patient seemed at first to do well. The membrane gradually separated, and on the 11th the throat was clear of membrane. Some ulceration on fauces. On the 14th began to vomit food. This continued on 15th. Heart became weak and patient died at 10 P.M.

CASE IX.—Clifford B——, aged one, son of Cora B——; died. Clinical history: Sick three days. Pharynx, tonsils, and cavities of nose lined by a thick, offensive, adherent pseudo-membrane. Croupy. Patient is cyanotic and septic, and very restless. Died at 1.10 P. M.

CASE X.—George B——, aged thirty; father. Clinical history: Has had for one day sore throat, pains in limbs, and prostration. Whole right tonsil is covered by a thick, soft, grayish smear, which can easily be removed, leaving adherent follicular deposits. Slight adherent patch on right anterior faucial pillar.

March 8th.—Merely follicular deposits on tonsil and slight membrane on anterior pillar.

March 14th.—Throat clean, except small patch on right anterior pillar.

March 17th.—Throat clean. Feels well.

Bacterial examination: All four cases gave such typical smears on cover-glasses of the Loeffler bacilli that an almost certain bacteriological diagnosis could be immediately made of true diphtheria. Besides the Loeffler bacilli, all had many colonies of a streptococcus which grew rapidly without forming looped colonies. In hanging drop it grew in short chains and as diplococci. The plates showed colonies of numerous other varieties of cocci and bacilli.

Guinea pigs were inoculated from cultures of eight and ten. The animals died in seventy-two and twenty-four hours with characteristic changes.

The history of the spread of the contagion in these cases is interesting. Two months before, a child living on the floor below them had what the doctor called diphtheria. Until a few days before the sickness of Cora B——, the two families had kept apart. For the last few days they had visited each other, and Cora had carried and played with the child who had recovered from the diphtheria. When the mother took sick she was still allowed to nurse and carry the children. Three days later, the children were discovered to have contracted the disease. The mother, too sick longer to nurse the children, confided their care to the father, who himself became infected. Antiseptic cleansing of the nostrils and throat was neither used in treatment nor prophylaxis in these cases, before their admission to the hospital.

CASE XI. February 23d.—Charles B——, aged thirty;

recovery. Clinical history: Both tonsils, faucial pillars, and base of uvula are covered by a firmly adherent, thick pseudo-membrane of grayish color. Diffuse infiltration of adjacent tissues of neck.

February 24th.—Membrane has extended forward over palate.

February 27th.—Membrane separating in large pieces.

February 29th.—Clean, except for superficial ulceration of mucous membrane of soft palate.

On first two days temperature was about 101° F., after that below 100° F. On the tenth day albumin appeared in the urine.

Bacterial examination: Cultures made from bits of membrane showed many colonies of the Loeffler bacilli, until the 29th, when they ceased to appear. There were always many colonies of the streptococcus present.

CASE XII. February 25th.—Gustav V—, aged twenty-one. Recovery. Clinical history: Thick adherent patches of pseudo-membrane on tonsils and lateral walls of pharynx. Membrane began to peel off on the 27th, and had all disappeared on the 29th. After the first day the temperature was normal. Most abundant colonies are of the Loeffler bacilli; some colonies of streptococci present. After the 29th no more Loeffler bacilli present.

Guinea-pig inoculated died in seventy hours, with usual conditions.

CASE XIII. February 16th.—Mary C—, aged twenty; malignant; death. Clinical history: Has been sick two days before admission. Tissues of pharynx and palate swollen and cedematous. Whole of uvula, tonsils, part of soft palate, and part of pharynx covered by a thick, adherent, dirty gray pseudo-membrane. Much swelling of tissues of neck. The breath has a foul, sweetish odor. Patient is much depressed. Temperature, 98° F.; pulse, 100; respiration, 28. The pharynx, tonsils, and soft palate became one swollen mass covered by sloughing membrane. Swallowing difficult. For the last two nights patient was delirious and restless.

February 20th.—Pulse became rapidly weaker, and death occurred. Bacterial examination: Plates showed many varieties of bacteria, of which the Loeffler colonies comprised about one-third. Streptococci, micrococci, and bacilli were present.

CASE XIV. March 24th.—Polly K—, aged thirty; malignant; recovered. Clinical history: Sick two days. Pharynx, tonsils, and soft palate swollen and cedematous. Tonsils, faucial pillars, and part of soft palate covered by a rotten, grayish-green, adherent pseudo-membrane. Great prostration. Temperature, 101.4° F.; pulse, 100; respiration, 20.

March 25th.—Condition unchanged. Temperature, 99.4° F.

March 29th.—Membrane nearly disappeared. Condition improved. Three children of this patient died. Bacterial examination: Many colonies of the Loeffler bacilli, many of the streptococci and others.

CASE XV.—Child, aged six weeks; death; private practice. Clinical history: On first day small adherent patch on left tonsil and on base of uvula, also a piece of membrane hanging down from naso-pharynx, membrane spread over pharynx, and on third day into larynx. Child died on the fifth day. Glands were never swollen, and temperature did not rise above 99° F. until a few hours before death. The day before the illness of the child was noticed the mother was discovered to have diphtheria, and the child immediately removed, but too late. The mother went through a severe illness, also without fever, but recovered. Bacterial examination: An almost pure culture of Loeffler colonies on plates. No streptococci.

Animal inoculation: Guinea-pig died in fifty hours, with fairly characteristic lesions.

CASE XVI.—Child, aged two; recovery. Clinical history: Adherent gray patches, first on tonsils, then on pharynx and roof of soft palate. On seventh day spread to larynx and caused great dyspnoea. Calomel fumigations given every hour. Child never seemed very ill, except for the dyspnoea. Temperature never above 100° F. Glands not swollen.

Bacterial examination: The majority of the colonies were those of the Loeffler bacilli. Numerous colonies of micrococci were also present. No streptococci found.

CASE XVII. February 13th.—Child, aged six; private practice; recovered. Clinical history: When first seen tonsils were swollen. Next day adherent patches seen on tonsils. Tonsils became clean five days later. Some days afterward child was noticed to limp, and slight paresis of muscles of left side was found. In the next house, the week before, there was a case of clinical diphtheria, and this child played with the children from the other house.

Bacterial examination: Many colonies of Loeffler bacilli and many scattering forms.

CASE XVIII. April 25th.—Minnie M——, aged twelve. Abscess tonsil; diphtheria. Comes from an asylum from which three others with diphtheria have been received. Has complained of sore throat for two days. Both tonsils and left peritonsillar region swollen and hyperæmic. Adherent patches on left tonsil, follicular deposits on right. Temperature, 102° F.; pulse

90; respiration, 24. Abscess in left tonsil ruptured and discharged a large amount of pus at the moment of examination. Recovered entirely by fourth day. Cultures gave numerous colonies of the Klebs-Loeffler bacilli and of long-chained streptococci.

Guinea-pig inoculated died in forty-four hours, with characteristic lesions. Plates and tubes from tissue at point of inoculation gave abundant colonies.

CASE XIX. February, 1892.—Child, aged six weeks; private practice; death. Clinical history: Began with bloody discharge and membrane in nose. Membrane spread to pharynx, tonsils, and larynx. Death about the tenth day. Father of child had been attending diphtheria cases.

Bacterial examination: Cultures from a piece of membrane gave abundant colonies of the Loeffler bacilli and of the long-chained streptococcus. A piece of membrane taken three days later from the nose gave very numerous colonies of the staphylococcus pyogenes aureus. Guinea-pig died in forty-eight hours, with characteristic lesions, after inoculation with the bacilli.

CASE XX. February 13th.—Henry K.—, aged sixteen. Clinical history: For one week a room-mate had been sick with diphtheria, swabs from whose throat gave an almost pure culture of the Klebs-Loeffler bacilli. On first day of his illness both tonsils and adjacent borders of pillars were covered by a thick, soft, dirty pseudo-membrane. The pharynx and fauces were swollen and deeply injected. Temperature, 103° F.; pulse, 120. Glands swollen.

February 14th.—The tonsils still swollen and painful, but the diffuse membrane disappeared, leaving only croupous patches confined to the tonsils.

February 17th.—Small follicular deposits still remain.

February 18th.—Tonsils clean, though still swollen.

There was never any albumin in urine. Temperature and pulse sank to normal on the second day.

Bacterial examination: Very numerous colonies of the Loeffler bacilli, some streptococci.

CASE XXI. March 23d.—Cornelius V.—, aged seven. Clinical history: Tonsils, anterior faucial pillars, and roof of soft palate covered by a thick, grayish-white, adherent membrane. Temperature, 101° F.; pulse, 120. Marked swelling in adjacent tissues of neck. Considerable prostration.

March 27th.—Membrane peeling off. Glands of neck less swollen. Temperature, 100° F.; pulse, 130. Prostration still marked.

March 29th.—Expelled a large piece of membrane from nose.

April 1st.—Throat clear. Temperature, 98.6° F.; pulse, 130. Made a slow recovery.

Bacterial examination: Very abundant colonies of Loeffler bacilli and many streptococci.

CASE XXII. March 23d.—John V——, aged five, brother of previous case. Clinical history: Slight adherent patch on left tonsils. Hardly complains at all. Temperature, 100° F.

March 25th.—Patch smaller.

March 27th.—Throat clean. Feels well.

Bacterial examination: Cover-glasses show many typical Loeffler bacilli, of chain cocci and diplococci. The cultures from both cases contained many colonies of the Loeffler bacilli, streptococci, and micrococci.

The previous week the oldest sister had croupous inflammation of the tonsils and soft palate. The children were not isolated. The second child had absolutely no symptoms. Treatment with spray and douche of 1 to 4,000 bichloride solution was begun probably a few hours after infection.

CASE XXIII. February 17th.—Gussie G——, aged three and a half; diphtheritic rhinitis; recovery. Clinical history: Slight deposits on left tonsil. Obstruction to nasal breathing and dirty discharge from the nose.

February 21st.—Small adherent patches still on tonsils. Glands on left side of neck swollen and painful.

February 23d.—To-day a large, thick, fibrinous pseudo-membrane, four inches in length, was washed from the nose. It was a partial cast of both nostrils. Patient doing well. Tonsils almost clean.

On the 25th scarlet fever developed, from which she finally recovered. Temperature never rose over 101° F. until the development of the scarlet fever.

Bacterial examination: From the pharynx the culture showed many typical colonies of the Klebs-Loeffler bacilli. From the membrane from the nose only a very few colonies were obtained, among which were a few of the Krebs-Loeffler bacilli and a few of the streptococci.

Membranous Rhinitis.—CASE I.—January 19, 1892. Roosevelt Dispensary. Service Dr. Jonathan Wright. Aged three. Recovery. Clinical history: Right nostril occluded by a thick succulent membrane. Left shows in front small adherent deposits. Upper lip eczematous with a few pustules. Bloody secretion from nose. Pharynx and larynx free. Temperature by rectum, 100° F.; pulse, rapid. Removal of a piece of membrane caused considerable bleeding. Patient never seemed really ill. On the fifth day the nostrils were free from membrane. Still considerable discharge and swelling. No albumin in urine.

Bacterial examination: Cover glass preparations from

membrane showed cocci, diplococci, and bacilli, among which were some fairly typical Loeffler bacilli. Cultures contained numerous colonies of Loeffler bacilli and of the long-chained streptococci and of a few other micrococci.

Guinea-pig inoculated with 1 to 2 c.c. of bouillon culture, second generation, of the Loeffler bacilli, died on the fifth day, with characteristic lesions. A rabbit was inoculated in the ear with 1 to 2 c.c. of a bouillon culture, two days old, of the streptococci. On the second day rabbit's temperature was 102° F.; the ear about inoculation somewhat reddened. On third day temperature 103° F., considerable redness and oedema of the whole central half of ear was present. The temperature and local signs of inflammation then subsided.

CASE II.—Gertrude B——, aged four. Discharge and occluded nostrils for six days; peevish; anæmic. Both nostrils filled in front by a thick, succulent, adherent, light-gray membrane. Free hemorrhage on removal. Pharynx clear of deposit. Temperature, pulse, and respiration nearly normal. Urine, 1.007, clear, no albumin or casts. On sixth day membrane separated.

CASE III.—Tom Mc——, aged four and a half. Vanderbilt Clinic, service Dr Simpson. Discharge and occluded nostrils one week. Both nostrils filled by thin, grayish-white, adherent pseudo-membrane. Temperature, 100° F.; pulse, 130. Urine, 1.010, clear; no albumin or casts. Nostrils clear sixth day.

CASE IV.—Ellen B——, aged eighteen months. Roosevelt Dispensary. For six weeks has had an otitis media. For one week discharge from nose. On septum and turbinated bones thin, grayish-white, adherent membrane. Child seems well. Membrane all disappeared on fifth day.

CASE V.—E. W——, aged five. Same history as previous cases. Membrane separated sixth day. Never appeared sick.

CASE VI.—Mary B——, aged three. Membrane separated sixth day. Never appeared seriously ill.

In all the latter five cases of membranous rhinitis quite numerous colonies of the Klebs-Loeffler bacilli were present, in three associated with streptococci, and in two with staphylococci. From the first four, guinea-pigs were inoculated. One died on the fifth day and one on the seventh. The other two appeared sick for a few days and then recovered. In the neighborhood of the inoculation some induration could be felt. The slight virulence of the bacilli is remarkable.

These cases are very interesting. Like those observed by all other observers they ran a benign course. The only precaution to prevent the spreading of the contagion was antiseptic irrigation. No history of infection was ob-

tained in any. In all six cases the colonies of the Loeffler bacilli grew rather feebly, both on the blood-serum and on the agar. The bacilli from the agar were small and often pointed, from the blood-serum and broth long and slender, with swollen ends. The cultures died out more quickly than those from ordinary cases. The bacilli in the membrane were rather long and slender, with few clubbed forms.

Cases of Laryngeal Diphtheria Requiring Intubation.

Number.	Name.	Age.	Lesion.	Temperature, pulse, and respiration on admission.		Result.
1	Lizzie D...	16 mos.	Croupous laryngitis.	Temp., 102; pulse, 130; resp., 40.	Intubated 3d day; died 4th day.	Died.
2	Maggie D...	4 yrs.	Croupous laryngitis; slight patches tonsils.	Temperature, 101.6; pulse, 118; resp., 28.	Intubated before admission.	Died.
3	Margt. G...	1 yr.	Croupous laryngitis; tonsils and uvula.	Temp., 101; pulse, 150; resp., 56.	Intubated 4th day; died 6th day.	Died.
4	Lena G....	4½ yrs.	Croupous laryngitis; slight patches tonsils.	Temp., 102; pulse, 140; resp., 42.	Intubated 4th day; died 6th day.	Died.
5	Abram A...	2½ yrs.	Croupous laryngitis; tonsils. Pneumonia?	Temp., 104; pulse, 136; resp., 46.	Intubated before admission; died next day.	Died.
6	Ike S.....	18 mos.	Croupous laryngitis; bronchitis.	Temp., 100; pulse, 132; resp., 30.	Intubated on admission.	Recovered.
7	Charles H.....		Croupous laryngitis; scarlet fever.	Temp., 103.	Intubated on admission.	Recovered.
8	Female	4 yrs.	Croupous laryngitis; measles.		Intubated	Recovered.
9	Female	5 yrs.	Croupous laryngitis; tonsils and pharynx.		Intubated	Died.
10	5 yrs.	Croupous laryngitis; slight patches tonsils.		Intubated	Died.
11	2 yrs.	Croupous laryngitis.	Reported in histories of Cases No. 1-5.	Intubated	Recovered.
12	4 yrs.	Croupous laryngitis.		Intubated	Died.
13	2½ yrs.	Croupous laryngitis; pharynx and tonsils.		Intubated	Died.
14	1 yr.	Croupous laryngitis; pharynx and nostrils.		Intubated	Died.

Whole number of cases requiring intubation, 14, of which 10 died and 4 recovered. Ages varied between one and five years. In Case 8 the bacilli grew and appeared like those in the membranous rhinitis cases. In 6 of these no membrane was visible anywhere above the larynx. In 1 scarlet fever, and in 1 measles existed as a complication.

Table of Diphtheria Cases not Included in the List of Cases of Membranous Rhinitis and Laryngitis.

Number.	Sex.	Age.	Location of Pseudo-membrane.				Duration.	Result.
			Tonsils.	Palate.	Nose and pharynx.	Larynx.		
1	F.	6 years.	Follicular deposits.	1	Days. 6	Recovered.
2	M.	4 years.	Patches.	Recovered.
3	F.	6 years.	Patches.	1	1	4	Died.
4	F.	12 years.	Patches.	4	Recovered.
5	F.	10 years.	Follicular	1	4	Recovered.
6	F.	4 years.	Patches.	1	5	Died.
7	M.	4 years.	Patches.	1	4	Died.
8	F.	8 years.	Patches.	1	4	Recovered.
9	F.	6 years.	Patches.	1	1	5	Died.
10	F.	15 years.	Patches.	1	6	Recovered.
11	F.	16 years.	Patches.	1	1	5	Died.
12	M.	21 years.	Patches.	1	4	Recovered.
13	F.	4 years.	Deposits	1	6	Recovered.
14	F.	6 years.	Follicular	5	Recovered.
15	F.	30 years.	Patches.	1	8	Recovered.
16	F.	4 years.	Follicular	1	1	1	8	Died.
17	5 years.	Extensive	1	1	1	15	Died.
18	26 years.	Extensive	1	1	7	Died.
19	5 years.	Extensive	1	1	9	Died.
20	1 year.	Extensive	1	1	1	4	Died.
21	30 years.	Extensive	1	10	Recovered.
22	30 years.	Extensive	6	Recovered.
23	21 years.	Extensive	1	4	Recovered.
24	20 years.	Extensive	1	1	6	Died.
25	30 years.	Extensive	1	Pharynx.....	7	Recovered.
26	6 weeks.	Slight	Naso-pharynx..	1	5	Died.
27	2 years.	Slight	Recovered.
28	6 years.	Slight	1	Recovered.
29	5 years.	Slight	Recovered.
30	6 weeks.	Extensive	1	1	Died.
31	16 years.	Extensive	1	Died.
32	7 years.	Extensive	1	Naso-pharynx..	Recovered.
33	5 years.	Slight	Recovered.
34	5 months.	Slight	Naso-pharynx..	1	Died.

Résumé of Points of Interest in the Fifty-four Cases of True Diphtheria. (The reliability of cultures and of the immediate diagnosis from cover glass smears.)—In every case in which cultures revealed the Loeffler bacilli during any part of the disease the first examination disclosed numerous colonies. This would seem to show that cultures made from a fresh swab, or bit of membrane, can be thoroughly relied upon to show the presence or absence of the Loeffler bacilli as soon as the pseudo-membrane is developed. After the complete separation of the membrane they were in every case missed. In many cases an examination of cover-glass smears, when made from fresh swabs or membrane, gives an immediate reliable diagnosis. This requires great care and should always be controlled by cultures. Swabs from the pharynx of cases, in which no membrane was visible, also give knowledge of the bacteria infecting the larynx.

Methods of Spreading the Contagion.—Cultures made from the dried stains on spreads, pillow-cases, and sheets, where soiled by the expectoration of diphtheria patients, showed, in every case, at least a few colonies of the Loeffler bacilli. (See Photograph 4.)

We know by actual experiment that, under favorable conditions, when mixed with shreds of tissue and mucus, they live for many weeks. The sputum of patients, though apparently not containing any bits of membrane, is yet usually crowded with them.

More than one third of the cases gave a clear history of having been brought in contact with the persons or clothes of those suffering from, or having recently had, severe pseudo membranous inflammations, diagnosed as diphtheria; and in eight the diagnosis had been verified by finding the Loeffler bacilli.

Case V. brings out strongly the manner in which diphtheria breaks out in unexpected places. The child, aged five, is taken out of town and left to sleep in an infected bed for a few hours, and dies ten days later. In another, a child is sent away for safety, but carries with him his infected clothes, and some of his playmates take the disease and die, while he himself escapes.

In another, five weeks before there existed diphtheria in the flat below. The first new patient taken sick was a child, aged two and a half years, three days later another, aged four, and then the mother herself. The children died, the mother went to the hospital and finally recovered. When she left home, her seven months' baby went to a friend's, where, three days later, two of the children developed diphtheria, and then finally the baby itself. The baby came to the hospital and died, one of the other children died.

Cases VII. to X. show the methods of transmitting the disease from one to the other. The sick mother carries the children and infects them. The father cares for them and is himself infected.

Physicians certainly are not careful enough to avoid carrying infection in their clothing, and to make sure that those whom they send from an infected house do not take it with them. In several of those in which the history of infection was investigated, great carelessness on the physician's part, in regard to warning those about the sick, was shown. The large number of cases of diphtheria which occur in the families of physicians should lead them to realize the danger of their carrying infection to others.

The practice, in hospitals for contagious diseases, of wearing gowns when examining patients, should be partially adopted by practitioners. The frequent crowded

condition of the diphtheria wards in the hospital forces the placing in the same room, and often in adjacent beds, those having true diphtheria and those not having it.

At first it would seem that the contagion must be carried from one to the other, but, as far as the Resident Physician knows, this has not taken place in the last two years, and it certainly never occurred during these investigations.

The great attention paid to cleanliness in the wards and the sterilization of instruments of examination account partly for this, but the routine cleansing of the nostrils and throats of all patients with a weak bichloride of mercury solution has also an important share in giving this freedom from infection. The important fact is that it seems possible to almost entirely prevent the spread of diphtheria if proper precautions are taken.

Age.—Of the 54 cases, 43 were under 10 years; 2 were under 8 weeks; 11 were adults.

Mortality.—Twenty-five died out of the 54; 4 deaths occurred in the 11 adults; 10 of the 14 cases requiring intubation died.

Effect of Treatment.—The patients that died in the hospital were, without exception, those that on admission had either very extensive membrane or laryngeal complications. In only three was there any extension of the disease after irrigation with 1 to 4,000 bichloride solution had been commenced. In a number of families where different members had had the disease for different lengths of time, those longest sick without treatment did badly, while those just attacked did very well. In these cases the virulence of the bacilli and the family predisposition were the same in both the early and later cases, so that the great difference in the course of the disease in the two classes was probably the effects of the treatment.

Location of Pseudo-membrane.—Of the 54 cases, in 6 the disease was confined to the nostrils, in 5 to the larynx and bronchi. In all others the tonsils were more or less involved. In bad cases the soft palate and uvula were extensively invaded. In the adults, the pseudo-membrane was generally thick, usually extensive, and of a dirty grayish color. In bad cases, the membrane became very thick and offensive. In some of the children the membrane presented the same appearance as in adults, while in others it was thin and grayish white, often simply in the form of little patches on the tonsils, uvula, soft palate, or faucial pillars.

Two cases with true diphtheria from an asylum, one appearing like a follicular tonsillitis and the other with an abscess of the tonsil, bring out the difficulty in making

a clinical diagnosis. In most of the mild cases in children this was impossible.

The severity of the disease seems to be almost directly in proportion to the extent of the membrane. The difference in cases is very striking. Those of croupous rhinitis, and many in which the disease is confined chiefly to the tonsils and uvula, both children and adults, hardly seem ill at all. Others with throat and nose lined with membrane are very seriously ill from the beginning and usually die.

The cause of the great difference in these cases is a very interesting study. It is certainly true that malignant cases usually propagate malignant ones, and mild cases mild ones. It is also true that now and then a severe case has received its infection from a mild one, and more frequently still, mild cases have come from severe ones.

The most plausible explanation seems to be that there is a great difference in the virulence of bacilli from different cases, and also that the degree of susceptibility of individuals varies greatly. Some seem almost to be immune. Whether the greater proportion of children infected is due to their greater susceptibility, or to the fact that they are so apt to put things in their mouths, and that, when carried, their faces are brought directly against that portion of the clothing most likely to be infected, is an interesting question.

In the limited number of cases here examined the effect of the association of other organisms cannot be safely judged. The opinion has been forced strongly upon me that the Loeffler bacillus is the predominating factor. Some of those having given pure cultures of the Loeffler bacilli have been fatal, while others in which streptococci abounded have been very mild. In malignant cases with sloughing membrane the surface is crowded with micrococci and bacilli, but the probability is that they find the dead tissue a good soil for their growth. In small children the association of the streptococci probably adds to the danger of a complicating broncho-pneumonia.

The temperature has been looked upon as a test by some. It is the general experience of those who have inoculated animals with Loeffler bacilli that the temperature falls soon after, and remains subnormal till death. On the other hand, inoculations of streptococci, when they produce any effect, raise the temperature.

In those cases of diphtheria in which the bacilli alone were present the temperature never rose above 100° F. In those in which the streptococci were abundant some had a high temperature, others a low. For prognosis the temperature was of no value except in children where lung complications occurred.

The marked swelling of the cervical glands and tissues was present only in those cases where other bacteria, especially streptococci were present. In many fatal cases there was no swelling, while some in whom it was marked recovered. In the bad cases, albumin in large amounts usually appeared in the urine. In many mild cases, no albumin was ever found. The deaths occurring some days after all membrane had disappeared from the throat bring out a peculiar danger in diphtheria.

The six cases of membranous rhinitis are of great interest, for it is only very recently that they have been thought to have any relation to true diphtheria. They seem regularly to recover.

Pseudo-membranous Inflammations in which the Klebs-Loeffler Bacilli are Never Present.—These will be considered in the following clinical divisions: 1. Extensive pseudo membranes, mostly confined to tonsils, soft palate, and pharynx: *a*, Uncomplicated; *b*, complicating infectious diseases. 2. Pseudo-membranes involving larynx (as only two of these were complicated by infectious diseases they will be considered with the uncomplicated cases). 3. Pseudo-membranes confined to the tonsils.

Extensive Pseudo membranes, Confined Chiefly to the Tonsils, Soft Palate, and Pharynx.—CASE I. February 5, 1892.—Polly D—, aged eight. Clinical history: Tonsils covered by large, irregular, adherent, whitish patches. Fauces and tonsils swollen, and livid in color. Temperature, 104° F.; pulse, 40; respiration, 20.

February 6th.—Tonsils, sides and tip of uvula, and faucial pillars covered by a thin, friable, grayish pseudo-membrane, which leaves a bleeding surface on removal. The appearance is as if on a mucous membrane denuded of its superficial epithelium a thick paint had been applied.

February 7th.—Tonsils and faucial pillars clear of membrane; superficial ulceration on pillars, and adherent membrane to uvula. Temperature remains between 102 and 104° F.; pulse, 118 to 130; respiration, 24 to 30.

February 16th.—Ulceration on uvula nearly healed. Temperature normal. No albumin in urine at any time. No great prostration.

Bacterial examination: Cultures were made daily from bits of membrane or swab, but never revealed any Loeffler bacilli. A quick-growing streptococcus which often appeared as a diplococcus was always the most frequent organism present.

CASE II. February 27th.—Charlotte V—, aged nineteen. Clinical history: Both tonsils, and adjacent

surfaces of uvula covered by a thin gray membrane. Tonsils much swollen and painful. Great hyperæmia of pharynx. Temperature, 99.6° F.; pulse, 100. No albumin in urine.

February 29th.—All symptoms abated. Membrane disappeared. No swelling of glands.

Bacterial examination: Almost pure culture of streptococci growing in long twisted chains.

CASE III. February 3d.—Rose L——, aged sixteen months. Clinical history: Thin, adherent, semi-transparent membrane on tonsils and adjacent surfaces of uvula. Nostrils occluded, but no membrane visible. Croupy voice and breathing. Slight swelling of glands of neck. Temperature, 100.2° F.; pulse, 136; respiration, 34.

February 4th.—Membrane nearly disappeared. Child nearly well.

February 6th.—Throat perfectly clean. Child is well. Evening temperature, 100° F.; pulse, 118; respiration, 28.

Bacterial examination: Almost pure culture of a streptococcus growing in long chains. A few colonies of a short-chain bacillus.

CASE IV. March 14th.—George M——, aged four years. Clinical history: Five days ago both tonsils removed. Now, on depressed stumps of tonsils, on anterior pillars, and on adjacent surfaces of the uvula is a very thin grayish membrane. Complains of sore throat and not feeling well.

March 8th.—Membrane has disappeared.

Bacterial examination: Plates and tubes gave a pure culture of a rapid-growing streptococcus, often appearing as a diplococcus.

CASE V. March 25th.—Woman, aged twenty-four. Case from Presbyterian Hospital. History of sore throat and pseudo-membrane for a week. Clinical history: Pharynx and tonsils swollen and livid red in color. Considerable pain on swallowing. Thin, flaky, whitish pseudo-membrane on the sides of the uvula, extending up a short distance on the soft palate, where the swelling has caused creases of the tissues, also similar-looking patches on the tonsils and pharynx. Temperature range, 100 to 101.5° F.

Bacterial examination: Many colonies of the long-chained streptococcus.

CASE VI. February 6th.—Margaret M——, aged twenty months. Clinical history: Uvula and lateral walls of pharynx covered by thin, adherent patches.

February 8th.—Still remain on uvula. Temperature varies between 99 and 101° F.

February 11th.—Throat clean.

Bacterial examination : Cultures reveal many colonies of the long chained streptococcus.

This case has an extremely interesting history. The child was exposed to scarlet fever for three hours just before its admission to the diphtheria wards of the hospital. On the eighth day the child developed scarlet fever. In two other cases, with similar throats, the children showed slight desquamation and are therefore considered as complicating scarlet fever. In this case the history excludes such a supposition.

CASE VII. February 3, 1892.—Gussie G——, aged nineteen. Clinical history : Hyperæmia of whole pharynx and tongue. Adherent thin grayish-white membrane on sides and tip of uvula. A few small grayish deposits on left tonsil. Temperature, 101° F. ; pulse, 98. On fifth day, no membrane ; feels well ; sixth day, discharged. Temperature, only on two days above 100° F. On the fourth day, trace of albumin in urine.

Bacterial examination : Cultures contained no colonies of the Loeffler bacilli, but many colonies of the long-chained streptococcus.

CASE VIII. February 3d.—Jennie K——, aged eighteen. Clinical history : Thin adherent pseudo-membrane on sides and tip of uvula. Some hyperæmia of pharynx. Temperature, 101.4° F. ; pulse, 100. Membrane remained four days. After the first day, temperature and pulse sank to the normal, and patient did not appear sick. No albumin in urine. Discharged on the sixth day.

Bacterial examination : Cultures revealed many colonies of the long-chained streptococcus and numerous others of various forms.

CASE IX. February 2, 1892.—Mary D——, aged twenty-one. Clinical history : For the past three days, pain on swallowing and on opening mouth. Posterior half of left tonsil, and post pillar, and most of uvula, covered by a thin grayish-white membrane, easily removed, leaving only a few bleeding points. No appreciable ulceration. Temperature, 102° F. ; pulse, 108 ; respiration, 26. Glands of neck on left side swollen.

February 25th.—Still thin white membrane on both tonsils and adjacent surfaces of uvula.

Bacterial examination : Plates and tubes gave a pure culture of the streptococcus.

Five other cases gave histories and lesions so similar to the above that it seems needless to give them in full.

Summary.—These fourteen cases present such uniform clinical appearances and histories that they deserve to be considered by themselves. The ages ranged from twenty months to twenty-one years. In no case was any

clear history of infection obtained, or of exposure to scarlet fever or measles. The considerable duration, three to eleven days, averaging five days, is important.

In these cases there is first a redness and swelling of the mucous membrane of the pharynx, tonsils, and fauces, with later a thin purulent discharge. Cultures at this time reveal very abundant colonies of streptococci. The epithelium of the inflamed mucous membrane, where the irritation is intensified by the contact and friction of adjacent surfaces, becomes necrotic, and the denuded surface becomes covered by a thin pseudo-membrane, composed mostly of streptococci held together by a small amount of fibrin. The streptococci may also penetrate into the denuded mucous membrane.

If one looks at a well marked case, having the patient open the mouth slightly, and depresses the tongue just a little, one will notice the inflamed uvula lying between and against the swollen tonsils. On the portions of the uvula thus irritated by contact, on the faucial pillars lying against the tonsils, and, in extreme cases, on the lateral walls of the pharynx and on the soft palate spreading up from the sides of the uvula, one finds this pseudo membrane which is always light grayish in color, thin, and friable. On removal, a bleeding surface is disclosed. When astringent applications are not used, the membrane usually disappears gradually, and does not scale off in firm pieces of considerable size, as in many cases of true diphtheria.

In none of these cases was there a fatal result; neither great prostration, after-emaciation, nor paralysis. Except that these cases were never complicated by suppuration of the cervical glands and diffuse cellulitis, they otherwise appear to be the same as the pseudo-membranous inflammations complicating scarlet fever, the greater severity in the latter being probably due to the influence of the scarlet fever. The temperature curve varied greatly in the different cases. In these fourteen cases the bacteriological diagnosis was of great value in prognosis, for pseudo-membranes, so extensive in true diphtheria, would have made it grave.

Pseudo-Membranous Inflammations Complicating Scarletina.—Confined chiefly to tonsils, soft palate, and pharynx. Seventeen of these cases were repeatedly examined. Except for complications, these gave exactly the same clinical appearances as those not complicating infectious diseases. Only six illustrative cases will be given.

CASE I. February 29th.—James F——, aged two and one-half. History of scarlatinal rash. Died. Clinical history: Slight desquamation on hands. There is a thin,

gray, adherent membrane on tonsils. Temperature, 100° F.

March 3d.—Thin, clean, grayish membrane on sides and tip of uvula.

March 7th.—Throat clean.

March 15th.—This child, with two others in the ward, to-day showed a re-formation of the membrane on tonsils and uvula.

March 16th.—Considerable laryngeal dyspnoea. Membrane persists.

March 18th.—Intubated. Bronchial râles over chest. Temperature, 101 to 103° F.; pulse, 130 to 150 ; respiration, 35 to 60 . Broncho pneumonia.

March 21st.—Left cheek and lip swollen and oedematous.

March 23d.—Extensive ulceration of mucous membrane of left cheek. Child very weak. Temperature and pulse remain high.

March 25th.—Tube removed. Membrane disappearing. Less swelling in face. Seems somewhat better.

March 31st.—Gradually grew weaker, with continued high temperature, until death.

CASE II. February 9th.—Frank McM——, aged two. Membranous rhinitis with pharyngitis. Death. Clinical history: Slight membrane on lateral walls of pharynx. Thick, whitish, succulent membrane blocking up both nostrils. Glands of neck swollen.

February 12th.—Marked increase in inflammation of glands and periglandular tissues. Pharynx clean. Disintegrating membrane in nose.

February 20th.—Glands suppurated. Had irregular high temperature, 102 to 105° F. Pulse above 150 . Died in septic condition.

Bacterial examination: Markedly twisted streptococcus, almost in pure cultures. No Loeffler bacilli ever present. Bouillon clear, with flocculent sediment.

CASE III. February 9th.—Edna K——, aged two and one-half. Death. Clinical history: Tonsils, adjacent edges of faucial pillars, and borders of uvula, covered by a thin, pearl-colored pseudo-membrane, which, when removed, reveals ulcerations. Rash. Temperature, 103° F.; pulse, 156 ; respiration, 34 . Patient died on the 18th with high temperature, pulse, and respiration.

Bacterial examination: Very numerous colonies of the long chained streptococci and nearly as many of the staphylococcus pyogenes aureus.

CASE IV. February 7th.—William W——, aged seven. Had had scarlet rash and high temperature. Recovered. Clinical history: On 18th, thin, whitish membrane adherent to tonsils. Glands of neck swollen.

February 27th.—Incision of suppurating glands. Tonsils clean.

February 29th.—Better in every way. Temperature remained between 99 to 101° F.

Bacterial examination: From throat and from glands a streptococcus, in long twisted chains, was obtained. From the thin purulent serum from the glands a pure culture was secured.

CASE V. February 23d.—Annie O'H——. Recovered. Clinical history: Scarlet rash; no fever; slight hyperæmia of throat.

March 17th.—When apparently well, developed a thin, dirty-white membrane on tonsils, which left a raw surface on removal.

March 19th.—Considerable ulceration of tonsils, and marked induration of glands of neck, with tenderness.

March 25th.—Membrane disappearing.

From swab of throat on February 23d nearly pure culture of the streptococcus longus. From bit of membrane, March 19th, almost pure culture of colonies of a streptococcus, appearing as a diplococcus and in short rows under the microscope.

CASE VI. February 18, 1892.—Rose C——, aged three and a half. Died. Clinical history: Child looks very ill. Thin, soft membrane on sides of uvula, anterior pillars, and lateral walls of pharynx. When removed, leaves bleeding, ulcerated surface. Glands of neck swollen.

February 21st.—Membrane nearly gone, superficial ulceration on sides of uvula. Glands hard, indurated, and much swollen. Died on 22d. Temperature varied between 103 and 105° F.; pulse, 160 to 170; respiration, 44 to 58.

Bacterial examination: Almost pure culture of the streptococcus.

Summary and Remarks.—In 11 other cases of similar soft membrane on faucial pillars, edges of uvula, and tonsils, by far the most numerous colonies were those of the long-chained streptococci. In one case a streptococcus, similar to that occurring in the late membrane in Case V., was present. From 2 cases of follicular tonsillitis, and from 8 cases, without exudation, in which hyperæmia of pharynx and scarlet rash were present, abundant streptococci were invariably found. In none of the cases were the Loeffler bacilli found. Of the 10 cases of scarlet fever, in which the complicating croupous inflammation appeared early, 6 died. In the 7 in which it appeared late, all recovered. In the 6 fatal cases, 2 had extensive gangrenous cellulitis, beginning in the neck, spreading over the chest, and causing the sloughing of an extensive

portion of skin. A third had diffuse suppuration in and about the cervical glands.

The presence of streptococci growing in long twisted chains in the throats of all the cases examined during the period of the eruption is very noteworthy, and strongly indicates the necessity of carefully looking after the cleansing of the throats, whether any visible membrane is present, or not. The fatal result in some seemed to be due more to the complicating cellulitis and abscesses than to the scarlatina. The possibility, suggested by some observers, that the streptococci may be the cause of scarlet fever, is worthy of investigation. It would take very strong evidence, and necessitate finding some constant differences between the streptococci occurring in scarlet fever and those appearing so frequently in other conditions, or the proof that they can at one time cause scarlet fever and at another a local lesion in the throat. It would seem more probable that the infectious diseases, especially scarlet fever and measles, favor the development and growth of the streptococci, known to be so frequently present in both the healthy and inflamed throat.

In three of the children who were entirely convalescent the pseudo-membranous inflammation seemed to be the result of an infection from others in the ward. The pseudo-membrane lining the nasal cavities in Case II. is interesting, indicating that some cases of membranous rhinitis are due to streptococci.

Pseudo-membranes Involving Larynx caused by Streptococci.—CASE I. February 13th.—Hattie S—, aged five. Recovered. Clinical history: On admission, cyanotic from laryngeal obstruction; intubated, relieved; very slight, adherent, thin, pearl-gray patches on uvula. Temperature, 100° F.; pulse, 102; respiration, 22.

February 17th.—Patient never seemed sick; exudation on uvula disappeared; no albumin in urine; tube remained in five days.

Bacterial examination: Plates and tubes, made on two days, showed no Loeffler bacilli, but many colonies of a long chained streptococcus and scattering forms.

CASE II. February 14th.—Nochem E—, aged six. Recovered. Clinical history: Admitted with marked laryngeal stenosis; intubation gave perfect relief; no membrane visible. Temperature, 101° F.; pulse, 132; respiration, 34. From time to time some difficulty in breathing, which was relieved by calomel fumigation. For one week temperature varied between 99 and 101° F.; pulse, 100 to 126. Never any visible membrane. No albumin. Tube removed on the fifth day.

Bacterial examination: No Loeffler colonies found on

plates or tubes made from swabs of pharynx and tonsils taken on the first three days; numerous streptococci.

CASE III. March 16th.—Osthof —, aged three and one half. Recovered. Clinical history: Admitted with marked laryngeal dyspnoea; vomited, was fumigated, but without relief; intubated; both tonsils covered by a nearly white, thin, adherent membrane. Temperature, 101° F.; pulse, 128; respiration, 30.

March 19th.—Still extensive patches of same membrane on tonsils; breathes fairly well; no prostration. On second day temperature reached 103° F. Now 99° F.

Bacterial examination: Numerous colonies of streptococci; none of Loeffler bacilli.

CASE IV. March 18th.—Esther F—, aged one. Recovered. Clinical history: Very small white patch, slightly adherent to right tonsil; laryngeal dyspnoea; made to vomit, and fumigated with calomel, but without relief; intubated five hours after arrival. Temperature, 99.6° F.; pulse, 120; respiration, 30.

March 20th.—Seems about well; tube still retained; some albumin in urine.

March 26th.—Tube removed; temperature never above 100° F.

Bacterial examination: Cultures gave abundant colonies of the long-chained streptococcus.

CASE V. March 19th.—Morris G—, aged four. Died. Clinical history: Intubated before admission. Temperature, 100° F.; pulse, 130; respiration, 32. No membrane visible in throat; some white, flaky membrane coughed up; large amount of albumin in the urine.

March 22.—Chest full of râles; child drowsy and cyanotic, although there is no laryngeal obstruction. Temperature, 102° F.; pulse, 150; respiration, 42. Swallows with difficulty. Died on 23d.

Bacterial examination: Abundant colonies of long-chained streptococcus and many of micrococci and other scattering forms.

CASE VI. March 21st.—Margaret F—, aged four. Clinical history: Marked laryngeal dyspnoea on arrival, intubated one-half hour later; large piece of thin, crumbling membrane coughed up through tube; swollen tonsils, with small whitish patches. Temperature, 99.4° F.; pulse, 104; respiration, 26.

March 24th.—Tube removed; seems well; highest temperature, 101° F. No albumin in urine.

Bacterial examination: Cultures from swabs and from membrane coughed up had many colonies of long chained streptococci and some of streptococci appearing in short rows and as diplococci.

CASE VII. March 30th.—Katie F—, fifteen

months, sister of last. Clinical history : Five days before admission slight cough, next night awoke suddenly with croupy cough. The laryngeal symptoms increased from night to night. Intubated shortly after admission. Temperature, 100.2° F. ; pulse, 112 ; respiration, 28. Thin whitish deposits on tonsils.

April 1st.—Had an attack of marked laryngeal dyspnoea, requiring the removal of the tube. Attached to it was a long piece of membrane. Temperature, 103° F. ; pulse, 144 ; respiration, 30. Restless.

Patient developed broncho-pneumonia. Temperature remained high. Tube was removed on the eighth day. Died on April 10th.

Bacterial examination same as in last.

These two cases occurring in the same family, one eight days after the other, point to the possibility at least of a direct transmission of the contagion.

CASE VIII. March 3d.—Jennie P—, aged eleven months. Intubation. Death. Clinical history : Slight patches on tonsils, laryngeal dyspnoea. Whole lower face badly burned, through attempt of mother to give it steam inhalations. Child looks badly. Moist râles over whole chest. Glands of neck slightly swollen.

March 4th.—Intubated. The tube keeps clogging with thick purulent fluid. Dyspnoea increased, and child died at midnight.

Bacterial examination : From first day many streptococci, and many colonies of a quick-growing micrococcus, which liquefied gelatine and coagulated milk. The growth on the media was entirely different from the staphylococci. From trachea, after death, an almost pure culture of the micrococci was obtained.

CASE IX. March 17th.—James F—, aged two and one-half. Intubation. Death. Clinical history : On account of a previous history of scarlet fever, this case has been described under the scarlatinal class.

CASE X. March 19th.—William M—, aged thirty. From Presbyterian Hospital. Clinical history : No specific, alcoholic, or nephritic history. Symptoms began on the morning of the day admitted. When admitted, patient was suffering from laryngeal dyspnoea. Examination revealed much swelling and redness of whole larynx, also a small patch of moist membrane on arytenoids.

March 21st.—Dyspnoea was so bad on the 20th as to nearly call for tracheotomy. To-day breathing easier. Soft, dirty-gray membrane persists on swollen arytenoids. Small patches, also, on the false cords and epiglottis. Membrane disappeared after two days, and patient recovered. The orderly who attended the patient developed a marked follicular tonsillitis. In both these cases

the most numerous colonies were those of the streptococcus growing in long twisted chains.

CASE XI. April 27th.—Andrew I——, aged forty-three. Death. On admission the history is obtained from friends that he has been three days sick. He is weak, slightly delirious, and appears as if suffering from some severe infectious disease. The whole uvula and the portions of soft palate adjacent to it are covered by a very thin, dirty covering which can hardly be called a pseudo-membrane. The whole pharynx and palate are extremely hyperæmic. Patient is hoarse, and has some laryngeal dyspnœa. Temperature, 103° F.; pulse, 128; respiration, 26. Patient became violently delirious, and died the next day. No autopsy.

This case is interesting as it is the only fatal one in adults. It is probable that the croupous inflammation was only a complication of some one of the infectious diseases.

*Pseudo membranous Laryngitis, not True Diphtheria.—
Table of Cases.*

Number.	Name.	Age.	Disease and complications.	Temperature, pulse, and respiration on arrival.	Length of time intubated.	Result.
1	Hattie S.	5 years.	Croupous laryngitis; croupous patch on uvula.	Temp., 100; pulse, 102; resp., 22.	Membrane remained 4 days; intubated for 5 days.	Recovered.
2	Nochem E.	6 years.	Croupous laryngitis.	Temp., 101; pulse, 132; resp., 34.	Tube removed 5th day.	Recovered.
3	Harry O.	3½ years.	Croupous laryngitis; croupous tonsillitis.	Temp., 101; pulse, 128; resp., 30.	Tube removed 5th day.	Recovered.
4	Esther F.	1 year.	Croupous laryngitis; croupous tonsillitis.	Temp., 99; pulse, 120; resp., 30.	Tube removed 8th day.	Recovered.
5	Rosie B.	3½ years.	Croupous laryngitis.	Temp., 99; pulse, 116; resp., 24.	Tube removed 3d day.	Recovered.
6	Morris G.	4 years.	Croupous laryngitis; broncho-pneumonia.	Temp., 102; pulse, 150; resp., 42.	Intubated before admission; lived 4 days.	Died.
7	Jennie P.	11 mos.	Croupous laryngitis; croupous tonsillitis; scald of face; bronchitis.	Temp., 103; pulse, 150; resp., 40.	Intubated with but slight relief; lived 1 day.	Died.
8	James F.	2½ years.	Extensive pseudo-membrane in throat; cellulitis; croupous laryngitis; broncho-pneumonia.	Temp., 100.	19 days after admission intubated; removed after 7 days.	Died.
9	Barney S.	2½ years.	Croupous laryngitis; developed measles 8th day.	Temperature, 101.4; pulse, 106; resp., 38.	Intubated; removed 8th day.	Recovered.

Pseudo-membranous Laryngitis, not True Diphtheria.—
Table of Cases.—Continued.

Number.	Name.	Age.	Disease and complications.	Temperature, pulse, and respiration on arrival.	Length of time intubated.	Result.
10	Wm. C...	2 years.	Croupous laryngitis; croupous rhinitis.	Temp. 101.4; pulse, 128; resp., 38.	Intubated; removed 8th day.	Recovered.
11	Bert. P...	4 years.	Croupous laryngitis.	Temp., 104; pulse, 144; resp., 48.	Intubated.	Recovered.
12	Kate F...	15 mos.	Croupous laryngitis; croupous tonsillitis; broncho pneumonia.	Temp. 100.2; pulse, 112; resp., 28.	Intubated; lived 11 days.	Died.
13	Margt. F.	4 years.	Croupous laryngitis; croupous tonsillitis.	Temp. 99.4; pulse, 104; resp., 26.	Intubated half an hour after admission; removed after 3 days.	Recovered.
14	Harris A.	3 years.	Croupous laryngitis.	Temp. 101; pulse, 144; resp., 40.	Intubated on admission; removed 6th day.	Transferred for measles 9th day.
15	Wm. F..	30 years.	Croupous laryngitis.	Moderately high temperature.	Marked dyspnoea.	Recovered.
16	Andrew J.	43 years.	Croupous laryngitis; pharyngitis, etc.	Temp., 103; pulse, 128; resp., 26.	Patient died in 24 hours; apparently had some infectious disease besides croupous inflammation.	Died.

Fourteen of these 16 were in young children. In 5 of the 16 no deposit or membrane was visible above the larynx. Four of the 5 deaths were due to lung complications.

Summary.—These sixteen cases, occurring in four months, prove that membranous croup is frequently an independent disease, having no connection with true diphtheria. In only two was any connection with scarlet fever or measles discovered. On admission, a diagnosis from clinical history and appearance was impossible.

In the majority of the ten cases that recovered, the course of the disease was mild. After intubation had relieved the dyspnoea, the patients never appeared dangerously ill. By the third day they were sitting up in their beds and playing with their toys. The temperature averaged somewhat higher during the first days than in the cases of laryngeal diphtheria, and rose to 103 and 104° F. when the lungs became involved.

In two of the children a pretty clear history of direct infection from other cases was obtained. In croup, the magical effect of intubation is seen, for without trache-

otomy or intubation the majority would certainly have died. The good percentage of recovery, $71\frac{1}{2}$ per cent., in these cases, as contrasted with intubation in diphtheritic laryngitis, $28\frac{1}{2}$ per cent., throws much light on the problem why at certain times and in certain countries the percentage of recoveries is so much greater than in others. It also forces the query whether, in the future, all cases should not be examined bacteriologically, if the statistics are to be valuable. Broncho pneumonia seems to be the most frequent cause of death.

Pseudo-membranes Confined to the Tonsils Caused by Streptococci.—CASE I. March 3, 1892.—Genet M—, aged six. Clinical history: From an asylum with three other cases. Right tonsil is swollen and covered by a thick, adherent, gray-colored, fibrinous pseudo-membrane. Cervical glands considerably swollen on right side. Slight pain and tenderness. Temperature, 101° F.

March 5th.—Still thick membrane on tonsil. Nowhere else. Feels well.

March 7th.—Tonsil clean. Is slightly croupy.

March 9th.—Perfectly well.

Bacterial examination: Cover-glass made from smear of membrane showed very numerous cocci in pairs, singly, and in chains. Also a few bacilli. Plates gave an almost pure culture of the long-chained streptococcus. Nothing found in anyway similar to the Klebs-Loeffler bacillus.

CASE II.—Mark C—, aged four. From same asylum. Clinical history: Pseudo-membrane on upper portion of left tonsil and adjacent surface of anterior and posterior pillars. Well on third day. No fever.

Bacterial examination: Mostly streptococci.

CASE III. March 5, 1892.—Lottie E—, aged twenty-one. Clinical history: Both tonsils are nearly covered by irregular, semi-adherent pseudo-membranous patches. Considerable swelling and hyperæmia. No swelling of glands. Not much pain; slight constitutional symptoms. Temperature, 101° F.

March 7th.—Tonsils nearly clean. Feels well.

March 8th.—Perfectly well.

Bacterial examination: Many colonies of the long-chained streptococcus and other scattering forms.

CASE IV. March 12th.—Charles F—, aged thirty. Clinical history: Two days ago felt pain and soreness in region of tonsils. Went to Bellevue, and was sent to Charity Hospital. From there taken to the Willard Parker Hospital. Both tonsils covered by a dirty-brownish smear which is readily removed, leaving irregular patches on tonsils. Pharynx covered by thick, purulent discharge. Tonsils and peritonsillar tissues are

much swollen, and the whole pharynx and fauces hyperæmic. Considerable swelling of glands of neck. Temperature, 102° F. Great pain on swallowing and on opening mouth.

March 14th.—Still considerable swelling and hyperæmia, but membranous deposits have nearly disappeared. Feels much better.

Bacterial examination : Reveals mostly colonies of the long-chained streptococcus.

CASE V. March 13th.—Mary C——, aged four. Clinical history : This child is from the same asylum in which four cases occurred ten days before. Both tonsils are swollen, and covered by thick masses of exudate. Temperature, 101.4° F.

March 16th.—Tonsils are clean. Patient feels well.

Bacterial examination : Plates give nearly pure cultures of the long-chained streptococcus.

CASE VI. March 14th.—Annie E——, aged six. Clinical history : Both tonsils covered by irregular patches of pseudo membrane, with intervening portions smeared with purulent discharge. Considerable swelling of tonsils. Almost no constitutional disturbance.

March 16th.—Tonsils almost clean.

Bacterial examination : The great majority of the colonies are of streptococci.

CASE VII. March 7th.—George M——, aged thirty-one. Clinical history : Felt chilly and depressed two days ago. The next day his physician on examination found the tonsils swollen and covered with a semi-adherent soft deposit. He was referred to the Board of Health. The first examiner thought it a doubtful case, referred it to a second, who pronounced it true diphtheria. On admission, condition the same. Glands of neck somewhat swollen.

March 8th.—Throat is clear, and he feels well.

Bacterial examination : Majority of colonies, streptococci in long twisted chains.

CASE VIII. March 11th.—Land F——, aged twenty-two. Clinical history : History of recurrent attacks of sore throat similar to present one. Swollen, irregularly excavated tonsils, with a few irregular, gray deposits. Pain on swallowing and opening mouth.

March 14th.—Right tonsil nearly covered by dirty adherent pseudo membrane. Left, follicular deposits. Less pain and tenderness.

March 16th.—Still small deposits on tonsils.

March 18th.—Tonsils clean.

Bacterial examination : The most numerous colonies are of a rather quick growing streptococcus which occurs as a diplococcus and in short chains of diplococci.

Summary.—This disease is so familiar that it is unnecessary to give more illustrative cases. In the 159 here studied 58 are included under this heading. This comparatively large number would seem to indicate that in adults, thick croupous patches, adherent or not adherent, if confined to the tonsils, after twenty-four hours very rarely have anything to do with true diphtheria. The same bacteria (the streptococci) which under certain influences cause an inflamed throat or a follicular tonsillitis, under others seem to produce a croupous tonsillitis. In several cases two members of a family were affected, one with the former, the other with the latter disease. In a few others a very complete history of direct transmission of the contagion was obtained. The croupous deposit, or pseudo membrane, lasted from two to seven days. All cases recovered without complications.

The intimate connection of some cases of croupous tonsillitis with scarlet fever is brought out in the following examples :

Rose F—, aged twenty-one, was admitted, with marked croupous tonsillitis with constitutional and local symptoms, on May 20th. The three previous days she had taken care of a child sick with scarlet fever, and on the last day also of the mother, who was attacked with croupous tonsillitis. Both she and the mother had come in frequent direct contact with the child.

Two physicians attended a gentleman sick with malignant scarlet fever and croupous tonsillitis. Both were attacked with croupous tonsillitis, and one with scarlet fever also.

The streptococci, found in the pseudo-membranes, presented some striking differences. By far the most frequently present was a streptococcus showing similar morphological and biological traits to the streptococcus pyogenes and erysipelatus. This streptococcus was present in all the scarlatinal cases during the eruption. From the different cases the cultures presented some minor differences in the size of the colonies and the appearance of the flocculi in the broth. The pathogenic qualities varied greatly. Inoculations in rabbits from some produced abscess and necrosis, from others merely slight redness and swelling.

During the last two months, cultures from a number of cases presented a coccus which formed larger colonies than the long-chained streptococcus on the agar plates, producing colonies with nearly even edges, of a coarse, granular, and blotched appearance. Here and there, from their edges short runners sprouted out, and in some cases short twisting loops.

In bouillon, at 37° C., the growth of this streptococcus

is vigorous, forming, in twenty-four hours, considerable gray sediment, with cloudy bouillon. Microscopical examination reveals diplococci in pairs and short rows of four to eight. In gelatine tubes the growth does not differ from that of the streptococcus pyogenes except in that it is somewhat more vigorous. The few animal experiments made indicated it to be less pathogenic than the long chained streptococcus in rabbits. Injected in the ears of rabbits it produced redness and swelling, from the second to the fifth day, with very slight or moderate fever. The rabbits after the fifth day seemed well. Intravenous inoculation was without effect in two cases. A third variety differed only from the first, in that the loops were less twisted. One of these forms, usually the first, was the most abundant micro-organism present in every one of the cases examined, in which the Klebs-Loeffler bacilli were absent. And in cases of true diphtheria they were usually present in greater or lesser numbers.

The staphylococcus pyogenes aureus was only irregularly present in the cases examined, and only abundant in five. In these, from the blood-serum tubes alone one would have judged that they were the most abundant form of bacteria, but an early inspection of the plates under the microscope revealed the tiny colonies of the streptococci to be present in far the greater number.

In those cases in which suppuration of the cervical glands and extensive cellulitis was present, the long-chained streptococci were always found, except for such complications the special form of streptococci present seemed to exert no influence on the severity or length of the disease.

General Summary.—*Bacteria.*—In 159 cases of pseudo-membranous inflammations there were 54 in which the Klebs-Loeffler or diphtheria bacilli were present, usually as the only or most numerous form of bacteria. With them were often associated streptococci and other micro-organisms. In every one of the remaining, streptococci were the most abundant bacteria, and often the only ones. From various pseudo membranes the streptococci obtained differed in manner of growth and pathogenic action. The staphylococci were often entirely absent, at other times present in moderate numbers, but never in excess of the streptococci.

Location of Lesion.—In both diphtheria and pseudo-diphtheria the pseudo-membranes occurred on the mucous membrane of the nose, pharynx, larynx, soft palate, and tonsils. In both, the tonsils were the parts most frequently involved. The nasal cavities were more often involved in true diphtheria.

Mortality.—In true diphtheria, $46\frac{1}{2}$ per cent.; in pseudo-diphtheria, $5\frac{3}{8}$ per cent.; intubation in diphtheria, $71\frac{1}{2}$ per cent.; intubation in pseudo-diphtheria, $28\frac{1}{2}$ per cent.; adults in diphtheria, 36 per cent.; adults in pseudo-diphtheria, 2 per cent.

Contagiousness.—In quite a large proportion of cases evidence was obtained of the direct spreading of diphtheria through contact with infected persons and clothing. In only a few cases of pseudo-diphtheria was equally strong proof obtained. Children sent away from diphtheria for safety, carrying with them their infected clothing, were in a number of cases a source of danger to the families who received them.

Clinical Observations.—It is important at the outset to remember that true diphtheria is frequently associated with pseudo diphtheria, and this mingling of the two adds greatly to the clinical difficulties. Severe uncomplicated pseudo membranous laryngitis may be either true or pseudo diphtheria. The early clinical diagnosis is usually impossible. Low temperature, great prostration, and heart failure point to true diphtheria. A high temperature, lung complications, and no history of infection are in favor of pseudo-diphtheria.

Death occurred usually early, due to heart failure in diphtheria; usually later, due to broncho-pneumonia, in pseudo-diphtheria. In both, early death from suffocation may occur, if intubation or tracheotomy is not performed.

Membranous rhinitis is usually a very mild form of diphtheria having a good prognosis. Membranes complicating scarlet fever are seldom true diphtheria. Pseudo-membranes and thick deposits well developed on, but confined to, the tonsils of adults are nearly always pseudo-diphtheria. Follicular deposits confined to the tonsils in adults are probably always pseudo-diphtheria. Small or large, thick or thin, firmly or slightly adherent patches confined to the tonsils or extending to the larynx in young children may be either true or pseudo-diphtheria, and the clinical diagnosis is often impossible during any time of the disease. Extensive thin, grayish pseudo-membranes, occurring only on those surfaces of the uvula, tonsils, and faucial pillars which lie in contact were always pseudo-diphtheria. The prognosis is good in these cases, except when there are early complications of infectious diseases.

The thick grayish or grayish-yellow pseudo-membranes which cover a large portion of the soft palate and tonsils, often involving naso-pharynx and nostrils, were always the lesion of true diphtheria. These cases were often fatal in both children and adults.

Conclusions.—The results of previous investigations, with the addition of that brought out in these studies, seem to force on us the conclusion that there are two great divisions of pseudo-membranous inflammations, one caused by the Klebs-Loeffler bacilli and the other by some form of streptococci. The few cases in which the pneumococcus of Fraenkel or other cocci seem the cause naturally fall in the second division.

The first is, from beginning to end, a local process, and its lesions are due to the effects of the poison formed by the bacilli in the pseudo membrane. It is dangerous at all periods of life. The second is also at first a local lesion, but may at any time become a general infection. It is peculiarly liable to cause broncho-pneumonia in children. Both diseases are frequently associated together. Both are directly contagious, though in different degrees.

These two diseases, caused by different bacteria and differing in so many points, should no longer be called by the same name. The name diphtheria will probably be agreed upon by all for those cases in which the Klebs-Loeffler bacilli are present, whether alone or associated with other bacteria.

For the second division some name will have to be agreed upon; whether the streptococcus will be found to be in such a majority the cause that the name streptococcus diphtheria can be applied to it, only further investigation can determine. Perhaps at present the term pseudo-diphtheria will be acceptable.

In all cases where the diagnosis is in doubt, bacteriological examination should be made, because:

1. A correct diagnosis should always be sought for.
2. Without it, all attempts to learn from statistics the worth of special forms of treatment and methods of prevention are well-nigh useless from the frequent incorrectness of the diagnosis. The fact that during four months less than one-third of the cases sent to the diphtheria wards of the hospital had true diphtheria, is sufficient proof of the difficulty of making a clinical diagnosis.
3. It is a great help to prognosis and rational treatment in the more severe cases and enables us to take measures more effectually to prevent the spread of the contagion.
4. It is certain, can frequently be made immediately, and always within twenty hours.

The amount of familiarity with bacteriological work and the appliances necessary, although not very great, are still enough to prevent the great majority of physicians from undertaking it themselves. As the early detection of diphtheria is important for the general health, and as

this disease occurs most frequently and is most dangerous among the crowded poor, who are unable to pay for special examination, it would seem peculiarly the business of the Boards of Health to undertake it. In small cities some central place could be selected where the necessary appliances could be kept, in large cities several would be necessary. From these laboratories a properly equipped man could be called to make the cultures and give the bacteriological diagnosis. Children's hospitals and those for infectious diseases should certainly give their pathologist the means to do this.

To insure the safety of those not having diphtheria, these hospitals should have wards separated, where doubtful cases could be kept for twenty-four hours until the diagnosis was made certain by bacteriological examinations. Where this is impossible, experience at the Willard Parker Hospital has shown that general cleanliness and antiseptic irrigation of the nasal and pharyngeal mucous membranes is sufficient in the great majority of cases to prevent the spreading of diphtheria. Care should be taken not to expose small children to pseudo-diphtheria, for it is undoubtedly contagious under favorable conditions and is in them dangerous.

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128 WEST ELEVENTH STREET, July 1, 1892.

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